



Figure.

No ABO-I).

Conclusion: In this large study of mostly myeloablative, T-cell deplete, allogeneic transplant patients the presence of donor vs recipient Minor ABO-I did not significantly impact critical long term outcomes.

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Impact of Daptomycin Minimum Inhibitory Concentration (MIC) on Outcomes of Patients with Hematologic Malignancies and Hematopoietic Stem Cell Transplant (HSCT) Recipients with Vancomycin-Resistant Enterococci (VRE) Bloodstream Infection (BSI)

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Background: VRE is a common cause of BSI and daptomycin is often used as first-line therapy. The Clinical and Laboratory Standards Institute (CLSI) defines VRE isolates with daptomycin MIC (D-MIC) of ≤ 4 mg/L as susceptible. Clinical significance and treatment outcomes of VRE BSI episodes with D-MIC of 4, compared to those with D-MIC of 2 is currently undefined.

Patients and Methods: A single-center retrospective chart review of adults with hematologic malignancies and HSCT (autologous and allogeneic) recipients diagnosed with VRE BSI between September 2006 and September 2014 was performed. D-MICs were determined using Etest and VRE isolates with MICs < 2 or > 4 were excluded from the study. Only the first VRE BSI episode per patient was included.

Results: 53 BSI episodes were identified in 59 patients (27 allogeneic and 3 autologous HSCT; 29 with hematologic malignancies); of which 47.2% (25 of 53) and 52.8% (28 of 53) were due to isolates with D-MICs of 4 and 2 respectively. The median duration of bacteremia (4 versus 3 days; $p = 0.20$), median duration of neutropenia (15 vs. 17 days; $p = 0.78$), and Pitt Bacteremia Score ($p = 0.51$) did not differ significantly between patients with VRE BSI due to D-MICs of 4 and 2. The all-cause 30-day mortality after onset of BSI was 44.4% (D-MIC: 4) vs. 55.6% (D-MIC: 2) in HSCT recipients and 33.3% (D-MIC: 4) vs. 55.6% (D-MIC: 2) in patients with hematologic malignancies. 100% of the episodes were due to *Enterococcus*

faecium, with central venous catheters identified as the most common source of BSI. Daptomycin monotherapy was the most common treatment choice, used in 80% (47 of 59) of the BSI episodes.

Conclusion: The all-cause 30-day mortality, duration and severity of bacteremia did not appear to be different between VRE BSI episodes with D-MICs of 4 versus 2 in HSCT recipients and patients with hematologic malignancies.

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Alpha/Beta T-cell Depleted Allogeneic Stem Cell Transplantation from Matched Related and Unrelated Donor Grafts in Patients with Poor Risk Leukemia

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Introduction: The outcome of allo-SCT in patients with poor risk leukemia is still hampered by GVHD and relapse. The innate immune system has been reported to contribute to tumor control, with lower incidence of GVHD. Specific depletion of $\alpha\beta$ T-cells – key players in the development of GVHD – will render NK cells and gd T cells within the allograft. Recently reported results have shown the great promise of this approach in haploidentical transplantations. Within this study, we aim to extend $\alpha\beta$ T-cell depleted allo-SCT to patients with a MRD or MUD.

Methods: Patients with either 'poor-risk' or 'very poor-risk' leukemia were included in this phase I study. Either HLA matched siblings (MRD) or HLA matched (9 or 10/10) unrelated donors (MUD) were eligible. abT-cell reduction was performed by negative selection with anti-abTCR antibodies in combination with magnetic microbeads, using the automated CliniMACS device (Miltenyi Biotec, Bergisch Gladbach, Germany). The maximal contamination with abT-cells for all dose levels was 5×10^5 /kg. The conditioning regimen consisted of: ATG (Genzyme®) 4 or 6 mg/m² + fludarabine 120 mg/m² + busilvex AUC=90 followed by $\alpha\beta$ T-cell depleted grafts from matched related or unrelated donors. No additional immune suppression was given after allo-SCT.

Results: Products for 15 patients have been successfully processed and used for $\alpha\beta$ T-cell depleted allo-SCT between 2013 and 2014. A ~ 4 log depletion of $\alpha\beta$ T-cells has been observed in the product with a recovery of $\sim 75\%$ of CD34⁺ cells. The combination of ATG/fludarabine/busilvex was well tolerated with a hematological recovery within 3 weeks. Primary engraftment (chimerism $> 95\%$) was observed in all patients. Immune reconstitution primarily consisted of innate cells (NK cells and gd T cells) the first 6 months post

transplantation. In addition, no increase in CMV or EBV reactivations has been observed so far under the profound “innate control.” Up to date, none of the patients developed aGVHD > grade II.

Conclusion: ATG Busulfan Fludarabine is a low toxicity platform for abTCR-depleted transplantations, resulting in a swift reconstitution of innate cells (NK cells and gd T cells) the first 6 months post transplantation. This transplantation strategy can serve as a tool for future immunological interventions such as a pre-emptive DLI or transfer of genetically modified T cells.

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Role of Hematopoietic Cell Transplantation Co-Morbidity Index (HCT-CI) in Selection of Conditioning Regimen for Patients Undergoing Allogeneic Hematopoietic Cell Transplantation (Allo-HCT) – a Single Institution

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Objective: To compare Overall Survival (OS), Treatment Related Mortality (TRM), and Relapse Rate (RR) between myeloablative conditioning (MAC) and reduced intensity conditioning (RIC) regimens in patients with high/intermediate risk disease status. The hypothesis to be tested is that HCT-CI can be effectively used to decide on the preference of conditioning regimen and that RIC will decrease TRM without increasing relapse so that OS will be improved even in high/intermediate risk disease status patients with high HCT-CI.

Patients and Methods: Patients with high HCT-CI (≥ 3) underwent RIC regimen and those with low HCT-CI (≤ 2) underwent MAC regimen despite high/intermediate risk disease status. We analyzed the outcome of 92 patients with high or intermediate risk disease status (CIBMTR criteria) who underwent Allo-HCT at our institution between the years 2009 and 2013 inclusive. RIC regimen consisted of IV Fludarabine 30mg/m²/day infused over 30 minutes for 5 days on days -6 through -2 and IV Busulfan 3.2 mg/kg/day on days -3 and -2 (infusion rate 80 mg mg/hour). MAC regimen consisted of IV Fludarabine 50mg/m²/day infused over 1 hour on days -6 through -2, IV Busulfan 3.2mg/m²/kg/day on days -5 through -2 (infusion rate 80mg/hr), and TBI 200 cGY on days -2 and -1. All patients received Thymoglobulin at a total dose of 4.5 mg/kg or 6 mg/kg administered in divided doses on days -2, -1 and 0. Post-transplantation graft versus host disease (GVHD) prophylaxis consisted of tacrolimus and mycophenolate mofetil. Diagnoses included Acute Lymphoblastic Leukemia (n=4), Myeloproliferative disorder (n=7), Hodgkin's Lymphoma (n=8), Myelodysplastic Syndrome (n=20), Acute myeloid leukemia (n=25), and Non-Hodgkin's Lymphoma (n=28). Median age of the recipients was 52.1 years. The HCT-CI was high (≥ 3) in 41 recipients (47%) and 75 patients (83%) were in high risk disease status.

Results: At a median follow up of 13.2 months, the OS for patients undergoing RIC was 74.3% compared to 38.1% with MAC ($p=0.014$). The cumulative incidence of TRM at 12 months was 27.6% in patients undergoing MAC compared to <1% in RIC ($p=0.041$). Relapse related mortality at 12 months in RIC (25.7%) compared to MAC (50.5%) was not statistically different ($p=0.206$).

Conclusion: Our data demonstrates that use of HCT-CI is a simple but effective way to appropriately stratify patients with high/intermediate disease risk status to a particular conditioning regimen. The use of RIC in patients with high HCT-CI is non-inferior to MAC with our institutional data showing RIC is associated with low TRM, improved OS

without any statistically significant increase in mortality from disease progression or relapse. Prospective studies are necessary to validate these findings.

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Outcomes of Allogeneic Hematopoietic Cell Transplantation (AHCT) for Multiple Myeloma (MM): Impact of Disease Risk and Conditioning Regimen

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Background: AHCT remains the only curative option for MM despite improved survival with novel agents. We analyzed our single center experience of AHCT in MM over the past decade and examined factors associated with outcomes.

Methods: The outcomes of 77 consecutive MM patients receiving allotransplants from matched sibling (n=69) or unrelated donors (n=8) between 2002 and 2013 at our institution were analyzed. The primary objectives were to compare overall survival (OS), progression free survival (PFS), and non-relapse mortality (NRM) in patients based on biologic disease risk and conditioning regimen intensity. 60 pts. received allotransplant after non-myeloablative regimens (regimen 1) – low dose 200-cGy total body irradiation (TBI) +/-Fludarabine (n=52) or Cyclophosphamide + Fludarabine (n=8) while 17 received higher intensity conditioning (regimen 2) consisting of Fludarabine + Melfalan 140 mg/2 (11) or Cyclophosphamide + TBI (6).

Results: Patient, disease and transplant related characteristics are given in Table 1. Median follow up of survivors was 49.4 months. 27 (35.1%) had high-risk cytogenetics – t (4:14), 17p deletion, Chr 1 abnormality, or t (14:16). 96% had prior auto transplant with 17(22%) relapsing after auto transplant.

On multivariate analysis, older age (HR 1.06 95% CI 1.015, 1.120, $p=0.0112$), lack of a complete remission (CR) at allo-transplant (HR 0.15 95% CI 0.046, 0.485, $p=.0015$ in CR), longer interval from autologous transplant to AHCT (6.0 m vs. 5.2 m) (HR 1.04, 95%CI 1.008, 1.072, $p=0.01$) and CMV reactivation (HR 3.2, 95% CI 1.41, 7.52, $p=0.005$) were significant for higher mortality. CR at the transplant was associated with superior PFS (HR for treatment failure 0.332, $p=0.041$). Increasing age (HR, 1.07 $p=0.047$) and non-CR status at transplant (HR for CR - 0.164, 95% CI .035, .770, $p=0.021$) were associated with higher NRM. High-risk-disease and conditioning intensity were not associated with outcomes (Fig 1, 2).

Conclusions: The adverse effect of high-risk genetics may be overcome by the allogeneic effect irrespective of conditioning intensity. Allotransplant benefited younger patients and those in CR at the time of transplant and with short intervals from prior auto-grafts. No plateau in survival was demonstrated.